REMARKS

Claims 17-55 are withdrawn by the Examiner as being drawn to a non-elected invention. Claims 2-3 and 13-14 are withdrawn by the Examiner as being drawn to a non-elected species. Claims 1, 4-12, and 15-16 are examined.

Objection to the Specification

The disclosure is objected to because of embedded hyperlinks. By way of the above amendment, the embedded hyperlinks are removed. The disclosure is also objected to because the citation of US Patent 388 is incomplete. By amendment, the reference to US Patent 388 is removed. Applicants respectfully request withdrawal of the objection.

Claim rejections- 35 USC 112

Claims 1, 4-12, and 15-16 are rejected under 35 USC 112, first paragraph, for lack of written description in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner states that there is "no definition as to what constitute a precursor or what makes a precursor of a binding partner" (see Office Action, page 4). The Examiner further states that "Except for the general term disclosed in the specification, not a single precursor is described in the specification, let alone, a motif derived from said precursor" (see Office Action, page 4). Finally, the Examiner states that the specification fails to provide an adequate written description for step b of the claimed invention, and that the "exemplification drawn to step b of the claimed invention is nil" (see Office Action, page 5).

Applicants respectfully traverse.

The PTO has the burden of giving reasons, supported by the record as a whole, why the specification as a whole would lack recognition by persons skilled in the art of a written description of the invention defined by the claims (*In re Wertheim et al.* (CCPA 1976) 541 F2d 257, 191 USPQ 90). An applicant's disclosure need only reasonably convey to the skilled artisan that as of the filing date of the application relied upon, the applicant had possession of the specific subject matter claimed. It is further noted that according to the MPEP, "there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed" (see MPEP 2163.03). It has also been recognized by the courts that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics...i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics," (Enzo Biochem, Inc. v. Gen-Probe Inc., 296 F.3d 1316; 2002 U.S. App. LEXIS 14328; 63 U.S.P.Q.2D (BNA) 1609).

With respect to the term "precursor", one skilled in the art would reasonably understand that the applicant had possession of the claimed subject matter. Contrary to the Examiner's position that "not a single precursor is described in the specification", a non-limiting example of a precursor is clearly given on page 5, lines 18-19, as "polypeptides which may be modified post translationally". As is well-known in the art, post-translational modification of polypeptides is sometimes required to convert immature polypeptides into the active, mature form of a protein. Such post-translational modifications can include acetylation of side chains, hydroxylation of proline to hydroxyproline, phosphorylation of serine or threonine hydroxy

groups, glycosylation, or cleavage. As an example, proinsulin is modified post-translationally into insulin by enzymatic cleavage of the precursor after spontaneous folding of the immature polypeptide. One skilled in the art would immediately recognize that the inventor had possession of the claimed invention with respect to precursors based on the example of "polypeptides which may be modified post translationally". The functional language of a "precursor", combined with the structural example of "polypeptides", is sufficient to meet the written description requirement. No further definition is necessary, since a patent need not teach, and preferably omits, what is well known in the art.

With respect to step b of the claims, Applicant respectfully traverses the Examiner's statement that the "exemplification drawn to step b of the claimed invention is nil" (see Office Action, page 5). Step b of claim 1 comprises "comparing the identified amino acid sequence motifs to known amino acid sequences of a genome and identifying a gene product of said genome possessing said motif as the naturally occurring binding partner, or partner precursor, for said target". While not limiting the scope of step b, an example can be found on page 21, line 26 through page 23, line 17. A surrogate peptide known as KcB7 is identified by panning experiments, and then compared to known amino acid sequences of a genome, and found to reveal TNFR1 which is the natural biological partner of TNFβ. Such an example clearly demonstrates that rather than being "nil" as stated by the Examiner, the Applicants clearly had possession of the claimed invention. Therefore, Applicants argue that the Examiner has not met the burden of overcoming the "strong presumption" that an adequate written description is present in the specification as filed, and respectfully request withdrawal of the written description rejection.

Claims 1, 4-12, and 14-16 are rejected under 35 USC 112, second paragraph, as being indefinite. Claim 1 is rejected for omitting the essential step of "the method of identifying an amino acid sequence motif i.e., the step prior to screening or expressing amino acid sequences" (see Office Action, page 5). However, the Examiner's characterization of the method of identifying an amino acid sequence motif as being **prior to** screening or expressing amino acid sequences is incorrect. Rather, the method of identifying an amino acid sequence **comprises** the following steps of "screening a library comprising a plurality of different expressed amino acid sequences for binding of members of said library to the target; separating members of the library which bind to the target; determining the amino acid sequence of members of the library which bind to said target; and identifying as motifs common amino acid sequences among said determined amino acid sequences". Therefore, the claimed step is not omitted prior to the listed steps, but rather is described in the steps listed in part a.

Claim 1 is rejected for being indefinite as to the inconsistent use of the phrase "gene product" of the naturally occurring binding partner and protein. However, such inconsistencies are not pointed out by the Examiner. As the specification clearly states that the "term gene products encompass any post translational modifications" (page 5, lines 30-31), the standard of definiteness is met by the current disclosure.

The Examiner further rejects the claims, stating that the "metes and bounds of the claimed "precursor' is not clearly set forth in the claims or specification" (see Office Action, pages 5-6). However, the test of definiteness is whether one skilled in the art would understand the scope of the claim when read in the light of the specification. As such, a non-limiting example of a precursor is clearly given on page 5, lines 18-19, as "polypeptides which may be modified post translationally". While the term precursor is broad, breadth alone is not

indefiniteness. One of skill in the art is well-apprised of the metes and bounds of the term "precursor" in view of the specification.

Finally, claims 7 and 8 are supposedly "unclear as to the other sequences comprised in the 20 amino acids that would not materially affect the random sequence" (see Office Action, page 6). Applicants understand this rejection to be directed to the phrase "consists essentially of". However, section 2111.03 of the MPEP clearly indicates that "consisting essentially of" is an acceptable transitional phrase. According to the MPEP, "A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a 'consisting of' format and fully open claims that are drafted in a 'comprising' format". The Examiner's desire for "positive support in the specification, as to the other materials that do or do not materially affect the random sequence" is not necessary to meet the requirements of 35 USC 112, second paragraph. Rather, the MPEP only uses such language where an applicant contends that the phrase "consisting essentially of" overcomes the prior art.

Each of the rejections under 35 USC 112 having been addressed, Applicants respectfully request withdrawal of the rejections.

Claim rejections- 35 USC 102

Claims 1, 4-12, and 15-16 are rejected under 35 USC 102(a) as being anticipated by Blume et al (Biopolymers, 2000). While not conceding to the rejection, Applicants note that the date for the reference supplied on the previously submitted IDS, form 1449, was incorrect due to a clerical error. According to the publisher, the date of availability to the public through online publication was 1 February 2001, while dispatch of the reference to the public through the

mail was February 6, 2001 (see attached email from the publisher). Therefore, the reference is not available as prior art due to the priority date of May 9, 2000 of the instant application, based on Provisional Application 60/202,912. An updated IDS, form 1449, with correction of the clerical error, is attached. Applicants respectfully requests that the Examiner initial and sign the updated IDS.

Claims 1, 4-5, 9-12, and 15-16 are rejected under 35 USC 102(b) as being anticipated by Kraft (The Journal of Biological Chemistry, 1/22/1999).

The Examiner states that "Kraft basically discloses the same method steps as Blume above", and further that "Kraft uses RGD motif to identify the natural ligand, fibronectin that binds to the target αvβ6 of integrin with the motif as shown at Table III" (see Office Action, page 7). The Examiner states that claims 10 and 15-16 are disclosed on page 1979.

Applicants respectfully traverse the rejection. Kraft does not disclose a method of identifying a naturally occurring binding partner, or binding partner precursor, for a target. Specifically, Kraft does not identify a gene product of a genome as the naturally occurring binding partner, or binding partner precursor, for said target. While Kraft reports examples of human proteins containing the DLXXL motif in Table III, where the motif is shown to compete with fibronectin for binding to integrin, Kraft specifically states that the "possible biological relevance of such homologies remain unknown" (see page 1983, column 1, middle paragraph) and further that "we have no indication where, if at all, the xx-DLxxLx sequences play a biological role with αvβ6 integrin" (page 1984, column 2, second paragraph). Based on these two statements, it is clear that the authors were NOT using phage display coupled with amino acid sequence comparisons to find **naturally occurring binding partners**.

Furthermore, Kraft concludes that "the DLxxL peptides were not acting by competing for the β6 chain binding site on the αv chain" (see page 1984, right column, line 14). Also, the DLxxL peptides did not inhibit interaction of integrin with fibrinogen, one of the ligands identified as having the DLxxL motif. Finally, the peptides/motif identified by Kraft did not look like the naturally occurring binding partner fibronectin, whose interaction with integrin is inhibited. Taken as a whole, the facts show that the sequence of peptides from phage display as disclosed by Kraft do not resemble the natural partners whose interaction sites are contacted. Since Kraft cannot be said to disclose a method of identifying a naturally occurring binding partner, or binding partner precursor, for a target, Applicants respectfully request withdrawal of the rejection.

Claim rejections- 35 USC 103

Claims 1, 4-12, and 15-16 are rejected under 35 USC 103(a) as being unpatentable over Kraft in view of Kay et al (US Pat. 6,303,574). The Examiner admits that Kraft does not disclose a random sequence comprising about 20-40 amino acids or consisting essentially of about 20 or 40 amino acids. Examiner relies on Kay to remedy the deficiencies of Kraft, where Kay refers to random sequences of 9-45 amino acid residues encompassing a consensus sequence. The Examiner argues that the motivation for modifying Kraft comes from a motivation to produce a longer length random peptide in order to locate and fingerprint the motif "with high specificity and selectivity" (see Office Action, page 9).

Applicants respectfully traverse for the reason that neither publication teaches a method of identifying a naturally occurring binding partner, or binding partner precursor, for a target. The Kraft publication is discussed above, with the conclusion that Kraft lacks the claimed

method. Kay fails to remedy the deficiencies of Kraft because there is no mention of any homology, or even the possibility of homology to known binding partners. Furthermore, the references cannot be properly combined in that they are directed to non-analogous art. Kraft is directed to αvβ6 integrin proteins, while Kay is directed to SCR SH3 binding peptides

Additionally, obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion, or incentive supporting the combination. In the instant case, the publications cannot be combined because there is no motivation to combine them. The Examiner argues that motivation for modifying Kraft comes from a desire to produce a longer length random peptide in order to locate and fingerprint the motif "with high specificity and selectivity" (see Office Action, page 9). Kraft directly contradicts this motivation by truncating peptides, rather than lengthening them. Kraft states that "Truncation of the COOH terminus of DLxxL had little effect on inhibitory activity until the group at x^5 was deleted....Removal of the groups at x^1x^2 also abolished the activity, indicating that the core motif was the 8-amino acid sequence $x^1x^2DLx^3x^4Lx^5$" (see Kraft, pages 1982-1983). In practice, Kraft truncates peptides and finds no loss in activity with a core 8-amino acid sequence when compared to the larger sequence. Therefore, one of ordinary skill in the art would have no motivation to produce a longer length random peptide "in order to locate and fingerprint the motif with 'high specificity and selectivity'" as argued by the Examiner.

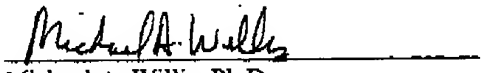
Conclusion

Each of the rejections having been addressed, Applicants respectfully request withdrawal of the rejections and allowance of all pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully invited to contact Michael A. Willis (Reg. No. P-53,913) at the telephone number of the undersigned below, to expedite prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required for the timely consideration of this amendment under 37 C.F.R. §§ 1.16 and 1.17, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2598-4004US1.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: May 29, 2003 By: 

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